REMARKS

The Office Action mailed October 26, 2007, has been received and reviewed. Claims 2 through 4, 6, 7, and 17 stand rejected.

The application is to be amended as previously set forth. All amendments are made without prejudice or disclaimer. No new matter has been added. Reconsideration is respectfully requested.

35 U.S.C. § 103 Obviousness Rejections

Obviousness Rejections Based on Cassol *et al.*, *Journal of Clinical Microbiology*, 1997, 35(11):2795-2801 in view of Cassol, *et al.*, *Mem. Inst. Oswaldo Cruz, Rio de Janeiro*, 1996, 91(3):351-358) and U.S. Patent 5,482,834 to Gillespie

Claims 2 through 4, 6, 7, and 17 are rejected under 35 U.S.C. § 103(a) as allegedly being made obvious by Cassol *et al.*, *Journal of Clinical Microbiology*, 1997, 35(11):2795-2801 (hereinafter "Cassol 1997") in view of Cassol, *et al.*, *Mem. Inst. Oswaldo Cruz, Rio de Janeiro*, 1996, 91(3):351-358) (hereinafter "Cassol 1996") and U.S. Patent 5,482,834 to Gillespie (hereinafter "Gillespie"). Applicants respectfully traverse the rejection.

A framework for applying the statutory language of §103 is set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966):

> "Under §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented."

Id. at 17–18. Prior art is not limited just to the references being applied, but includes the understanding of one of ordinary skill in the art. *Federal Register*, 72:195 (October 10, 2007) p. 57528. While the references need not teach or suggest all of the claimed limitations, the Office must explain why the differences between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art. *Id.* Furthermore, the Office examination guidelines published in response to *KSR* continually emphasize the importance of predictability.

Id. at 57529. While predictability by itself is not the only factor, 5 of the 7 rationales provided by the *KSR* court explicitly mention predictability of the solution as a factor. *Id.* Additionally, there must be "a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. _, 82 USPQ2d 1385, 1389 (U.S. 2007). Moreover, to establish a *prima facie* case of obviousness, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). Finally, the reason that would have prompted the combination and the reasonable expectation of success must be found in the prior art, common knowledge, or the nature of the problem itself, and not based on the Applicant's disclosure. MPEP § 2144. Underlying the obvious determination is the fact that statutorily prohibited hindsight cannot be used. *KSR*, 550 U.S. _, 82 USPQ2d at 1397.

Even if a *prima facie* case for obviousness were established by the Examiner (which Applicants dispute in this case), *Graham* set forth a broad inquiry and invited those making decisions as to patentability, where appropriate, to look at any secondary considerations that would prove instructive. *Id.* Secondary considerations include teaching away by others and recognition of a problem.

> "[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known."

Id. at 1389.

"A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning. *See Graham*, 383 U.S. at 36 (warning against a 'temptation to read into the prior art the teachings of the invention in issue' and instructing courts to 'guard against slipping into the use of hindsight'" (quoting *Monroe Auto Equipment Co. v. Heckethorn Mfg. & Supply Co.*, 332 F. 2d 406, 412 (CA6 1964)))." *KSR*, 550

U.S. _, 82 USPQ2d at 1397.

A *prima facie* case of obviousness under 35 U.S.C. § 103(a) has not been established because the combination of applied references actually teaches away from the presently claimed invention and, thus, one of ordinary skill in the relevant field would not have been motivated to combine the teachings of Cassol 1997, Cassol 1996 and Gillespie in the manner asserted. Additionally, the applied references themselves, or the inferences and creative steps that a person of ordinary skill in the art would have employed at the time of the invention, would not have taught or suggested the claim elements.

As amended, independent claim 1 recites "[a] process for preparing at least one sample for a method of detecting and quantifying a total amount of HIV nucleic acid present in the at least one sample, said process comprising: a) administering at least 100 microliters of the at least one sample to a piece of filter paper capable of absorbing the at least one sample, wherein the absorption results in at least one spot of the at least one sample on the filter paper, b) drying the filter paper having the absorbed at least one spot of the at least one sample, c) storing the filter paper for at least one week, d) excising the at least one spot of the at least one sample from the surrounding filter paper, e) extracting nucleic acid from the at least one spot of the at least one sample with a chaotropic nucleic acid isolation solution, f) detecting HIV nucleic acid, if present, and g) quantifying the total amount of the HIV nucleic acid present in the at least one sample."

One of ordinary skill in the art would not be motivated to combine the teachings of Cassol 1997, Cassol 1996, and Gillespie to produce the claimed process because Cassol 1997 teaches away from the asserted combination. Applicants note "the corollary principle that when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious." *KSR*, 127 S.Ct. at 1740.

As acknowledged by the Examiner, Cassol 1997 does not teach a process for quantifying a totally amount of nucleic acid in a 100 microliter sample. *See* Office Action, page 4. Rather, Cassol teaches using 50 microliter samples. The Examiner states that "it would have been obvious to detect total HIV-1 RNA, as taught by Cassol 1997, using similar methods of the Cassol 1996 reference." Office Action of October 26, 2007, page 4. At the time of the priority date of the present application, it was commonly taught in the art that only small volume samples of blood and plasma were suitable for quantification purposes. As provided in the as-filed

specification, high amounts of body fluid samples were not considered suitable for quantification of RNA because of perceived inhibitory effects. *See* as-filed specification, paragraph [0015]. Consistent with the teachings in the art and in the as-filed specification, Cassol 1997 teaches away from the use of large volume samples stating that "[w]ith samples with high copy numbers and large (200-µl) volumes, it is conceivable that the amplification reactions may become saturated." Cassol 1997, page 2799. Further illustrating the use of a small volume sample, Cassol 1997 teaches reducing the HIV Quantification Standard from 100 microliters to 25 microliters in order to compensate for the smaller 50 microliter volume of dried plasma used as a spot specimen. *See* Cassol 1997, page 2796, ¶3. Because Cassol 1997 teaches using small volume samples and, further, teaches the disadvantages of using samples having volumes larger than 50 microliters, it is respectfully submitted that one of ordinary skill in the art at the time of the present invention would have been led away from the asserted combination of Cassol 1997 and Cassol 1996.

Cassol 1996 does not quantify the total amount of HIV nucleic acid present in a sample and, thus, does not determine the viral nucleic acid load in a sample. Since sequencing a nucleic acid requires only a minimum amount nucleic acid, a large sample could be used in sequencing despite inhibitory effects. Accordingly, the fact that Cassol 1996 uses 2000 microliter spots in a method of sequencing would not have suggested to one of ordinary skill at the time of the present invention that larger volumes would be suitable for use in quantifying a total amount of HIV nucleic acid. Because Cassol 1997 teaches away from the use of samples larger than 50 microliters, one of ordinary skill in the art would not have found it predictable to utilize a sample size of 100 mL in quantifying a total amount of HIV nucleic acid.

In view of the inhibitory effects associated with the use of larger samples RNA quantification at the time of the present invention, such as those noted by Cassol 1997 and in the as-filed specification, one of ordinary skill in the art would not have had a reasonable expectation of success in using larger samples sizes, such as those taught in Cassol 1996, in a process for quantifying HIV-1 RNA.

It is further submitted that the applied references do not teach or suggest all of the elements of claim 1 because Cassol 1997, Cassol 1996 and Gillespie, alone or in combination, do not teach or suggest the element of "administering at least 100 microliters of the at least one

sample to a piece of filter paper capable of absorbing the at least one sample." Rather, Cassol 1997 teaches a method for HIV-1 viral RNA quantification that includes applying a 50 microliter aliquot of a plasma sample to filter paper. *See* Cassol 1997, page 2796. The Examiner acknowledges that Cassol 1997 does not teach or suggest using 100 microliters of sample for a single spot and, thus, relies on Cassol 1996 teaching the above-mentioned element of claim 1. *See* Office Action, page 4. However, Cassol 1996 teaches a method for direct automated sequencing of HIV-1 RNA using a 2 milliliter (2000 microliter) sample applied to filter paper. Gillespie teaches utilizing a chaotropic salt solution with nucleic acid probes. Therefore, Cassol 1996 and Gillespie cannot cure the deficiencies of Cassol 1997.

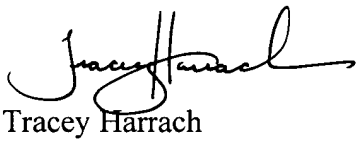
Applicants note that, '[t]he prior art reference (or references when combined) need not teach or suggest all the claim limitations, however, Office personnel must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art." M.P.E.P. § 2141 (III). The Examiner concludes that "since the 2000 microliter spot was adequate for quantifying particular HIV nucleic acid of interest, it is expected to also be adequate for total HIV-1 nucleic acid quantification." Office Action, page 4. However, no explanation has been given why it would have been obvious to one of ordinary skill in the art to use a 100 microliter sample in a process for quantifying a total amount of HIV nucleic acid. As such, it is respectfully submitted that *ex post* reasoning has been used in reading the teachings of the as-filed specification into the applied references.

It is, therefore, respectfully submitted that a *prima facie* case of obviousness has not been established against any of claims 2 through 4, 6, 7, and 17.

Reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) are respectfully requested.

The application should now be in condition for allowance. If, however, questions remain after consideration of the foregoing, the Office is kindly requested to contact Applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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